REMARKS

In the Final Official Action dated February 25, 2004, Claims 1, 3-11 have been rejected under 35 U.S.C. §112, first paragraph, as allegedly lacking enabling support. This response addresses the Examiner's rejection. Accordingly, the present application is in condition for allowance. Favorable consideration of all pending claims is respectfully requested.

Claims 1, 3-11 have again been rejected under 35 U.S.C. §112, first paragraph, as allegedly lacking enablement for prevention of injury to the myocardium or prevention of the onset of diabetic cardiomyopathy. Claims 1, 3-11 have also been rejected as allegedly lacking enablement for making and using the prodrug and salts of claimed compounds, or for use of the prodrugs and/or salts thereof in conjunction with additional compounds including the analogs, antagonists and agonists of the claimed additional compounds.

The Examiner maintains that Applicant's arguments and support in the specification presented in the previous office action failed to obviate the scope of enablement rejection but rather address a written description rejection.

Pursuant to the Final Office Action, the Examiner reiterated the reasons cited in the previous Office Action for the 35 U.S.C. § 112, first paragraph rejection; said reasons are quoted herein:

"Claims 1-11 are rejected under 35 U.S.C. § 112, first paragraph, because the specification while being enabling for treatment of diabetic cardiomyopathy, does not reasonably provide enablement for prevention of injury to the myocardium or prevention of the onset of diabetic cardiomyopathy, or how to make and use the prodrug and salts thereof, or for the use of the prodrugs and/or salts thereof in conjunction with additional compounds including the analogs, antagonists and agonists of the claimed additional compounds. The specification does

not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims."

The Examiner then asserted factors 1, 2, 4-7 of *In re Wands* as allegedly determinative that the disclosure does not meet the enablement requirement of 35 U.S.C. § 112, first paragraph. Moreover, the Examiner has taken the position that one skilled in the art would not be able to use the claimed compounds effectively without the need for undue experimentation.

The rejection under 35 U.S.C. §112, first paragraph is respectfully traversed.

It is well established, although not explicitly recited in 35 U.S.C. § 112, that in order to satisfy the enablement requirement statutorily defined therein, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 155; 27 U.S.P.Q. 2d 1510 (Fed. Cir. 1993). With respect to enablement, the relevant inquiry lies in the relationship between the specification, the claims, and the knowledge of one of ordinary skill in the art. *National Recovery Tech. v. Magnetic Sep. Sys. Inc.*, 166 F.3d 1190; 49 U.S.P.Q. 2d 1671 (Fed. Cir. 1999). The scope of enablement is that which is disclosed in the specification plus the scope of what would be known to one of ordinary skill in the art without undue experimentation. *Id.*, at 1675.

In traversing the rejection pursuant to 35 U.S.C. § 112, first paragraph, Applicants note that, although required for a § 112, first paragraph rejection, the Examiner has not stated specific technical reasons why one would not be able to extrapolate the examples of the present invention across the entire scope of claims. In the case at hand, the scope of the claims is as follows: Claims 1, 3-8 recite a method of treating or preventing diabetic cardiomyopathy with defined glycogen phosphorylase inhibitors; Claims 9-11 recite methods of treating diabetic

cardiomyopathy through administration of the defined glycogen phosphorylase inhibitors in combination with additional compounds.

It is incumbent upon the Patent & Trademark Office, whenever a 35 U.S.C. § 112, first paragraph rejection is made, to explain why it doubts the truth or accuracy of any statements in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement. *In re Marzucchi,* 439 F.2d 220, 224, 169 U.S.P.Q. 367, 370 (CCPA 1971). Here, no evidence which specifically refutes the pharmaceutical utility of the compounds of the present invention has been provided. Here, no reasons are advanced by the Examiner to establish that a person skilled in the art could not apply the examples in diabetic cardiomyopathy using the salts, prodrugs thereof in conjunction with additional compounds including the analogs, antagonists and agonists of the claimed additional compounds without undue experimentation. Here, no specific findings of fact, supported by the evidence have been provided. Nor has the Examiner identified what information is missing and why one skilled in the art could not supply the information without undue experimentation.

Applicants have pointed to the specification and examples and maintain that there is more than adequate disclosure to teach one skilled in the art how to prepare these compounds as well as how to use them without undue experimentation. One skilled in the art would be a highly skilled individual such as a physician, surgeon, or pharmacist. These individuals could easily grasp the concept defined in the specification without undue experimentation. The specification at pages 62-67 includes examples demonstrating glycogen phosphorylase production and assays; pages 67-68 include examples where the disease/condition-treating activities of the compounds of the present invention can be indirectly determined, i.e., glycogen phosphorylase activity assays permitting determination of an $IC_{50;}$ page 69 includes examples

where the compounds can be tested in animal models of diabetic cardiomyopathy including the streptozocin-induced diabetic rat, or the Syrian hamster; pages 69-71 include examples where the compounds can be tested in randomized double-blind clinical trials. These tests are applicable to the compounds claimed and detailed in the specification including the salts, prodrugs thereof in conjunction with additional compounds including the analogs, antagonists and agonists of the claimed additional compounds.

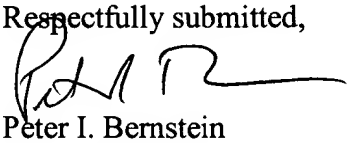
As a general matter, evidence of pharmacological activity will be relevant to an asserted therapeutic use if there is a reasonable correlation between the activity in question and the asserted utility. *Cross v. Iizuka*, 753 F.2d 1040, 224 U.S.P.Q. 739 (Fed. Cir. 1985); *In re Jolles*, 628 F.2d 1322, 206 U.S.P.Q. 885 (CCPA 1980); *Nelson v. Bowler*, 626 F.2d 853, 206 U.S.P.Q. 881 (CCPA 1980). Evidence of actual success in animal models and treating humans is not required and is reserved, in fact, to Food and Drug Administration Investigational New Drug (IND) and New Drug Application (NDA) review.

Moreover, it is respectfully asserted that the specification does in fact teach how to use and administer the claimed compounds of the present invention in the prevention and treatment of diabetic cardiomyopathy alone or in combination with other pharmacotherapeutic agents. Hence, Claims 1, 3-11 are clearly enabled.

It is, therefore, respectfully submitted that the specification clearly and unambiguously describes how to make and use the claimed compounds of the present invention as recited in Claims 1, 3-11. It is furthermore submitted that in light thereof the enablement requirement of 35 U.SC. § 112, first paragraph has been met and the rejection of these claims by the Examiner on this basis should respectfully be withdrawn and said claims be considered for allowance.

Thus, in view of the foregoing amendments and remarks, it is respectfully submitted that the present application is in condition for allowance. Accordingly, it is respectfully requested that this application be allowed and a notice of allowance be issued.

Respectfully submitted,



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